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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,580	04/24/2001	Andrea Califano	YOR920000687US2	5406

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/841,580

Applicant(s)

CALIFANO ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 17-19 and 23-25 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 17-19 and 23-25 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: ____.

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DETAILED ACTION

Applicants' arguments, filed 1 March 2004, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-3, 17-19, and 23-25 are currently pending.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Non-Statutory Subject Matter

Claims 1-3 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to **non-statutory subject matter**.

Applicant argues that "claim 1, from which claims 2 and 3 depend, recites deriving a transformation. The transformation renders uniform, within a selected interval, a distribution of transformed gene expression signals". Applicant asserts that a "derived transformation may be described as a non-linear similarity metric that maximizes the probability of discovering discriminative gene expression patterns." However, the fact remains that the **claimed** method to transform gene expression signals comprising determining the signals and deriving transformations using a function to create the transformation is only mathematical manipulation of the data generated from expression signals. A method which transforms gene expression

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signals to find certain patterns of expression MAY be one which produces a concrete, tangible, and useful result. However, some knowledge is required with regard to a specific patterns that result from such a method, for example. **In the instant claims**, there is no specificity identified as to what is intended by the outcome of the method. Therefore, the invention does not meet the standard of being immediately useful. Furthermore, there is no particular data identified or specific patterns recited in the specification such that a concrete, tangible, useful result is readily apparent. The specification is devoid of information on a possible correlation of this method to a particular disease or disorder for which this method may be useful or a particular phenotype, for example. There is no recitation of what to do with the probabilities generated or how that result of the method is concrete, tangible or useful.

As set forth in MPEP 2106: "For such subject matter to be statutory, the claimed process must be limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. See *Alappat*, 33 F.3d at 1543, 31 USPQ2d at 1556-57 (quoting *Diamond v. Diehr*, 450 U.S. at 192, 209 USPQ at 10). See also *Alappat* 33 F.3d at 1569, 31 USPQ2d at 1578-79 (Newman, J., concurring) ("unpatentability of the principle does not defeat patentability of its practical applications") (citing *O'Reilly v. Morse*, 56 U.S. (15 How.) at 114-19). A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible, and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible, and useful. See *AT&T*, 172 F.3d at 1358, 50 USPQ2d at 1452. Likewise, a machine claim is statutory when the machine, as claimed, produces a concrete, tangible, and useful result (as in *State Street*, 149 F.3d at 1373, 47 USPQ2d at 1601) and /or when a specific machine is being claimed (as in *Alappat*, 33 F.3d at 1544, 31 USPQ2d at 1557 (in banc))."

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Furthermore, not all processes are statutory under 35 USC 101, as put forth in *Schrader*, 22 F.3d at 296, 30 USPQ2d at 1460. To be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technical arts is either disclosed in the specification or would have been known to the skilled artisan or (B) be limited to a practical application within the technological arts.

Utility

Claims 1-3, 17-19, and 23-25 remain rejected under 35 U.S.C. 101 because the **claimed** invention lacks patentable utility.

Applicant argues that “the specification clearly teaches that transformations are derived, wherein a probability density distribution is transformed into a uniform probability.” However, the **claims** recite a method for transforming gene expression signals. The specification teaches that transformation of data can be used for identification of patterns in healthy verses unhealthy phenotypes such that these patterns may then be used to characterize an unknown sample into one of those two classes (page 6, lines 23-27; page 7, lines 1-2). However, the **claimed** method still is not directed to the steps of **classifying unknown samples into phenotype groups**. It is merely directed to transforming data that represent gene expression signals. The specification does not teach any specific, substantial, or well-established utility for a method that simply transforms expression signal data. Use of the claimed method to analyze the expression signals such that patterns are identified is certainly of scientific interest; however, no specific, substantial, and credible utility is set forth for the mere transformation of data as the “use” gained from this transformation is not disclosed or claimed. Utilities that require further research

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to identify or reasonably confirm a real-world context of use are not substantial utilities (See MPEP 2107.01). Therefore the claimed method does not have utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 17-19, and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 17, and 23 recite a method for transforming gene expression signals comprising “deriving a transformation that renders uniform, within a selected interval, a distribution of transformed gene expression signals for the gene”. It is still unclear what is meant by a “transformation that renders uniform”. The specification, at page 9, indicates that the nature of the invention is as follows: “to transform a probability distribution to a uniform distribution, an integral of the probability density function is performed.” This is not the same as the language of the instant claim. It is unclear in the instant claim that a probability distribution is being converted to a uniform distribution.

Claims 3, 19, and 25 still recite, “using the function to create the transformation, wherein the transformation renders uniform a probability distribution”. What function? It is unclear what is meant by rendering uniform a probability distribution. What are the parameters necessary to render a probability distribution uniform based on an unknown function?

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Claims 3, 19, and 25 recite, “wherein each gene expression signal is mapped by the transformation into a transformed gene expression signal”. Does applicant intend the transformation to actually map the signal? Applicant argues by pedantically offering a definition of “mapped” from Merriam-Webster’s Collegiate Dictionary. However it is still unclear, grammatically, how a transformation can “assign as a set or element in a mathematical correspondence.”

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 17-19, and 23-25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Eisen et al. (PNAS (1998) Vol. 95, pages 14863-14868), for the reasons set forth in the previous Office Action.

Applicant is reminded that in light of the 112, 2nd paragraph rejections above, the examiner is still applying the prior art based upon the broadest possible interpretation of the claims.

Applicant argues that Eisen does not “derive a transformation that renders uniform a distribution of transformed gene expression signals.” However, this is not persuasive. As stated previously, Eisen et al. teach a system of cluster analysis for genome-wide expression data from DNA microarray hybridization (see abstract, column 1). Data are collected on spotted DNA microarrays and images are acquired for each fluorescence (signal). Intensity ratios are measured and master data tables are formed for all experiments. All ratios are then **transformed** to treat inductions or repressions of identical magnitude. **Transformed** data, equal to G_i , is used to gain a similarity score. A mean observation is gathered and standard deviations calculated such that a Pearson correlation coefficient of the X and Y observations is calculated, meeting the limitations of transformation and probability distributions page 14864, column 1.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (571) 272-0549.

13 May 2003
Lori A. Clow
Art 1631

MARJORIE MORAN
PATENT EXAMINER

Marjorie A. Moran
5/13/04